Beta-ketothiolase deficiency

Description

Beta-ketothiolase deficiency is an inherited disorder in which the body cannot effectively process a protein building block (amino acid) called isoleucine. This disorder also impairs the body's ability to process ketones, which are molecules produced during the breakdown of fats.

The signs and symptoms of beta-ketothiolase deficiency typically appear between the ages of 6 months and 24 months. Affected children experience episodes of vomiting, dehydration, difficulty breathing, extreme tiredness (lethargy), and, occasionally, seizures. These episodes, which are called ketoacidotic attacks, sometimes lead to coma. Ketoacidotic attacks are frequently triggered by infections or periods without food (fasting), and increased intake of protein-rich foods can also play a role.

Frequency

Beta-ketothiolase deficiency appears to be very rare. Fewer than 250 affected individuals have been reported in the medical literature.

Causes

Mutations in the *ACAT1* gene cause beta-ketothiolase deficiency. This gene provides instructions for making an enzyme that is found in the energy-producing centers within cells (mitochondria). This enzyme plays an essential role in breaking down proteins and fats from the diet. Specifically, the ACAT1 enzyme helps process isoleucine, which is a building block of many proteins, and ketones, which are produced during the breakdown of fats.

Mutations in the *ACAT1* gene reduce or eliminate the activity of the ACAT1 enzyme. A shortage of this enzyme prevents the body from processing proteins and fats properly. As a result, related compounds can build up to toxic levels in the blood. These substances may cause the blood to become too acidic (ketoacidosis) and can damage the body's tissues and organs, particularly in the nervous system.

Learn more about the gene associated with Beta-ketothiolase deficiency

- ACAT1

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 2-methyl-3-hydroxybutyricacidemia
- 2-methylacetoacetyl-coenzyme A thiolase deficiency
- 3-alpha-oxothiolase deficiency
- 3-ketothiolase deficiency
- 3-oxothiolase deficiency
- Alpha-methylacetoacetic aciduria
- MAT deficiency
- Methylacetoacetyl-coenzyme A thiolase deficiency
- Mitochondrial 2-methylacetoacetyl-CoA thiolase deficiency - potassium stimulated
- Mitochondrial acetoacetyl-CoA thiolase deficiency
- T2 deficiency
- B-ketothiolase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Deficiency of acetyl-CoA acetyltransferase (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1536500/)

Genetic and Rare Diseases Information Center

- Beta ketothiolase deficiency (https://rarediseases.info.nih.gov/diseases/872/beta-ketothiolase-deficiency)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- ALPHA-METHYLACETOACETIC ACIDURIA (https://omim.org/entry/203750)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28beta-ketothiolase+deficiency%5BTIAB%5D%29+OR+%283-ketothiolase+deficiency%5BTIAB%5D%29+OR+%28alpha-methylacetoacetic+aciduria%5BTIAB%5D%29+OR+%28peroxisomal+thiolase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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